The Seventh International Symposium on Microsomes and Drug Oxidations will bring together the leading scientists in the world for discussions on the properties and functions of microsomal enzymes that are highly important for the inactivation and bioactivation of drugs, carcinogens, environmental pollutants and for the metabolism of normal body substrates. A better understanding of the properties and regulation of the microsomal enzyme systems that metabolize foreign chemicals will contribute to our understanding of the marked person-to-person differences that occur in the response of humans to foreign chemicals. The symposium will help advance the field of microsomes and drug oxidations by stimulating interactions between the participants and through the publication of the proceedings of the meeting.

ADDITIONAL INFORMATION

INTRODUCTION:

The purpose of this application is to solicit funds for the support of the Seventh International Symposium on Microsomes and Drug Oxidations. The cytochromes P-450 and related enzymes in liver microsomes and in extrahepatic tissues play a critical role in influencing the pharmacological and toxic effects of many foreign chemicals ingested by animals and human beings. These enzymes are also important for the metabolism of many lipid-soluble endogenous substrates such as steroids, sterols, fatty acids and prostaglandins. A better understanding of the structures, reaction mechanisms, functions, regulation, and molecular biology of these enzymes is highly desirable not only for promoting basic biomedical research but also for protecting human beings from hazardous effects of foreign chemicals such as drugs, food additives, pesticides, carcinogens and environmental pollutants.

The great interest in microsomes and drug oxidations stimulated the organization of six earlier symposia which brought together the foremost scientists in the field for discussions that resulted in increased interactions and collaborations among the scientists that attended the conferences and in the publication of the papers that were presented. The six earlier international symposia on microsomes and drug oxidations were held in 1968 (Bethesda, Maryland), 1972 (Palo Alto, California), 1976 (Berlin, West Germany), 1979 (Ann Arbor, Michigan), 1981 (Tokyo, Japan) and 1984 (Brighton, England). The publications that resulted from these six meetings were:

1. MICROSOMES AND DRUG OXIDATIONS, J.R. Gillette, A.H. Conney, G.J. Cosmides, R.W. Estabrook, J.R. Fouts and G.J. Mannering (eds.), Academic Press, New York, 1969.

2. THE SECOND INTERNATIONAL SYMPOSIUM ON MICROSOMES AND DRUG OXIDATIONS, R.W. Estabrook, J.R. Gillette and K.C. Leibman 1972.

3. MICROSOMES AND DRUG OXIDATIONS: PROCEEDINGS OF THE THIRD INTERNATIONAL SYMPOSIUM, V. Ullrich, I. Roots, A. Hildebrandt, R.W. Estabrook and A.H. Conney (eds.), Pergamon Press, Oxford, 1977.

4. FOURTH INTERNATIONAL SYMPOSIUM ON MICROSOMES AND DRUG OXIDATIONS, M.J. Coon, A.H. Conney, R.W. Estabrook, H.V. Gelboin, J.R. Gillette and P.J. O'Brien (eds.), 2 vols., Academic Press, New York, 1980.

5. MICROSOMES, DRUG OXIDATIONS, AND DRUG TOXICITY, R. Sato and R. Kato (eds.), Wiley-Interscience, New York, 1982.

6. MICROSOMES AND DRUG OXIDATIONS: PROCEEDINGS OF THE SIXTH INTERNATIONAL SYMPOSIUM, A.R. Boobis, J. Caldwell, F. DeMatteis and C.R. Elcombe (eds.), Taylor & Francis, London, 1985.

Three of the earlier symposia on Microsomes and Drug Oxidations were held as satellites to International Congresses of Pharmacology which facilitated the attendance of increased numbers of interested scientists. The Seventh International Symposium on Microsomes and Drug Oxidations will be held in Adelaide, South Australia, as a satellite of the Tenth International Congress of Pharmacology in Sydney.

AIMS OF THE CONFERENCE:

The aims of the conference are to bring together established leaders and young scientists working in the field of microsomes and drug oxidations to discuss their most recent work, to facilitate discussion and interactions between the participants, to stimulate the possibilities of collaborative research among the participants and to publish the proceedings of the symposium. Major themes for the symposium include (1) structural and immunological characterization of cytochrome P-450 isozymes, (2) cytochrome P-450 genes and their regulation, (3) human cytochromes P-450 and oxidative drug metabolism in human beings, (4) role of cytochrome P-450 in the metabolism of endogenous substrates, (5) post oxidation enzymes, and (6) metabolic activation and cell toxicity/carcinogenicity. The symposium will consist of plenary sessions and poster sessions.

DATES AND SITE OF MEETING:

The meeting will be held in Adelaide, South Australia from August 18-21, 1987, the week preceding the Tenth International Congress of Pharmacology in Sydney. All sessions will be held on the campus of the University of Adelaide.

ORGANIZING COMMITTEE:

The local organizing committee consists of Drs. Donald Birkett (Chairman), John Miners (Secretary), Felix Bochner, Ian Calder, Roger Drew, Brian May, Michael McManus and Andrew Somogyi.

INTERNATIONAL ADVISORY COMMITTEE:

The international advisory committee consists of Drs. A. H. Conney (U.S.A.), M. J. Coon (U.S.A.), D. S. Davies (U.K.), R. W. Estabrook (U.S.A.), Y. Fujii-Kuriyama (Japan), J. R. Gillette (U.S.A.), F. P. Guengerich (U.S.A.), E. F. Johnson (U.S.A.), R. Kato (Japan), U. A. Meyer (Switzerland), F. Oesch (F.R.G.), S. Orrenius (Sweden) and R. L. Smith (U.K.).

PROGRAM

The program was devised with the aim of updating our understanding of the microsomal enzymes that metabolize foreign chemicals and the normal body substrates for these enzymes. Particular emphasis will be placed on the regulation of the cytochrome P-450 genes in animals and man, hormones and cytochromes P-450, the chemistry and physics of cytochrome P-450, human cytochrome P-450 polymorphisms, functional correlates of cytochrome P-450 multiplicity in human beings, post-oxidation enzymes, metabolic activation and cell toxicity, and metabolic activation and carcinogenesis. The program for the symposium is given below:

DAY 1, TUESDAY, AUGUST 18

8.45 - 9.00	Welcoming/opening addresses:D.J. Birkett/Sato

PLENARY SESSION 1 - The polycyclic hydrocarbon inducible P-450 gene family in animals and man.

9.00 - 9.30	Levin (Nutley): Protein structure and inter-relationships of inducible P-450s. An overview.
9.30 - 10.00	Fujii-Kuriyama (Tokyo): Genes for the MC inducible P-450s in the rat.
10.00 - 10.30	Whitlock (Stanford): Regulation of MC inducible P-450s by the TCDD receptor
11.00 - 11.30	Hankinson (Los Angeles): The use of mutant somatic cell lines to characterize regulatory elements controlling P-450 expression.
11.30 - 12.00	Nebert (Bethesda): Genes for the MC inducible P-450s in mouse and man.
12.00 - 12.30	Tukey (San Diego): Genes for the MC inducible P-450s in rabbit (forms 4 and 6) and man.
12.30 - 1.00	Gelboin (Bethesda): Immunochemical studies of the MC inducible P-450s in man.
2.00 - 3.45	Posters/poster discussion sessions.

PLENARY SESSION 2 - The phenobarbitone inducible P-450 gene family in animals and man.

4.00 - 4.30	Kemper (Urbana): Genes for the PB inducible P-450s in rabbit.
4.30 - 5.00	May (Adelaide): Genes for the PB inducible P-450s in chick.
5.00 - 5.30	Adesnik (New York): Genes for the PB inducible P-450s in rat.
5.30 - 6.00	Phillips (London): Genes for the PB inducible P-450s in humans.

DAY 2 - WEDNESDAY, AUGUST 19

PLENARY SESSION 3 - Hormones, steroids and cytochromes P-450

8.30 - 9.00	E. Johnson (La Jolla): Regulation of the biosynthesis and catalytic function of steroid hydroxylases in rabbit.
9.00 - 9.30	Waterman (Dallas): Genetic regulation of adrenal steroid hydroxylases.
9.30 - 10.00	Omura (Fukuoka): Biosynthesis and processing of mitochondrial P-450s.
10.00 - 10.30	Perrin White (New York): Clinical disorders of adrenal P-450 deficiency.
11.00 - 11.30	Gustafsson (Huddinge): Role of growth factors in the regulation of hepatic P-450 expression.
11.30 - 12.00	Kato (Tokyo): Sex hormone dependent expression of P-450s.
12.00 - 12.30	Guzelian (Richmond): Glucocorticoid responsive P-450s in rat and man.
2.00 - 3.45	Posters/poster discussion sessions

PLENARY SESSION 4 - Chemistry and physics of cytochrome P-450.

4.00 - 4.30	Poulos (Gaithersburg): X-ray P-450 structure determination.
4.30 - 5.00	Sligar (Urbana): The use of site directed mutagenesis for the characterization of structure and function of P-450cam.
5.00 - 5.30	Groves (Ann Arbor): Mechanism of P-450 oxygen insertion.
5.30 - 6.00	Coon (Ann Arbor): The oxidation-reduction kinetics of P-450.

DAY 3 - THURSDAY, AUGUST 20

PLENARY SESSION 5 - Human P-450 polymorphisms

8.30 - 9.00	Guengerich (Nashville): Molecular basis for human P-450 genetic polymorphisms.
9.00 - 9.30	Gonzalez (Bethesda): Cloning of the human debrisoquine P-450 gene.
9.30 - 10.00	Meyer (Basel): Enzymatic basis of debrisoquine and mephenytoin polymorphisms.
10.00 - 10.30	Davies (London): In vivo/in vitro correlations for drug oxidation polymorphisms in man.

PLENARY SESSION 6 - Functional correlates of P-450 multiplicity in man.

11.00 - 11.30	Smith (London): Assessment of drug polymorphism in man.
11.30 - 12.00	Breimer (Leiden): Prediction of in vivo oxidative drug metabolizing activity in man.
12.00 - 12.30	Tucker (Sheffield): Pharmacokinetic and pharmacodynamic consequences of B-blocker oxidation polymorphism in man.
12.30 - 1.00	Birkett (Adelaide): Methylxanthines as probes for cytochromes P-450 in man.

PLENARY SESSION 7 - Glucuronosyltransferase

2.30 - 3.00	Tephly (Iowa City): Purification and characterization of GT isozymes in animals and man.
3.00 - 3.30	Mackenzie (Bethesda): Multiplicity of GT as revealed by gene cloning.
3.30 - 4.00	Bock (Gottingen): GT activities in preneoplastic liver.
4.00 - 4.30	Miners (Adelaide): Functional correlates of GT multipicity.

DAY 4 - FRIDAY, AUGUST 21

PLENARY SESSION 8 - Metabolic activation and cell toxicity

8.30 - 9.00	D. Ziegler (Austin): Flavin containing mono-oxygenase.
9.00 - 9.30	Ketterer (London): Multiplicity and distribution of glutathione-transferase.
9.30 - 10.00	Pickett (Rahway): Genes for glutathione transferases.
10.00 - 10.30	Mannervik (Stockholm): Role of glutathione transferase in chemical deactivation and activation.
11.00 - 11.30	Orrenius (Stockholm): Mechanisms of cell toxicity.
11.30 - 12.00	Ullrich (Konstanz): Inter-relationship between eicosanoid biosynthesis and xenobiotic activation.
12.00 - 12.30	Anders (Rochester): Reductive reactions of P-450 and cell toxicity.
1.30 - 3.15	Posters/poster discussion sessions.

PLENARY SESSION 9 - Metabolic activation and carcinogenesis.

3.30 - 4.00	Jerina (Bethesda): P-450 and the metabolic activation of polycyclic aromatic hydrocarbons
4.00 - 4.30	Kadlubar (Jefferson): Relationship between arylamine - DNA adduct formation and mutagenicity/carcinogenicity.
4.30 - 5.00	Harris (Bethesda): Polycyclic aromatic hydrocarbon-DNA adduct formation as a risk factor in human cancer.
5.00 - 5.30	Thorgeirsson (Bethesda): Post-oxidation events in chemical carcinogenesis.

5.30 - 6.00	Weinstein (Columbia): Activation of cellular oncogenes by chemical carcinogens
6.00	Closing comments (Birkett)

The following individuals have been proposed as chairmen of plenary sessions and as poster discussion chairmen.

1. Suggested plenary session chairmen:

Session 1: Conney/Beaune

Session 2: Oesch

Session 3: Silar-Masters/Estabrook

Session 4: Gunsalus

Session 5: Boobis

Session 6: Von Bahr

Session 7: Caldwel

Session 8: Moldeus/Gillette

Session 9: Adamson

2. Possible poster discussion session chairmen:

Jollow

Lu

Wilkinson

Inaba

Gorrod

Eichelbaum

Prough

PUBLICATION OF THE PROCEEDINGS

The proceedings of the previous six conferences have been published, and it is anticipated that the proceedings of the present conference will also be published.

ADMINISTRATION OF FUNDS

Rutgers University will administer the funds and reimburse U.S. speakers and chairpeople to the extent of $775 (U.S.) per person.

SIGNIFICANCE

Human beings are exposed to large numbers of foreign chemicals in the food he/she eats, the water he/she drinks and the air he/she breathes. In addition to the exposure of humans to large numbers of naturally occurring chemicals in the environment, humans are also exposed to many man-made chemicals. The cytochrome P-450 enzymes and related microsomal enzymes play an important role in metabolizing these chemicals to biologically inactive or toxic products so that the levels of these enzymes markedly influence the action of drugs, chemical carcinogens and a multitude of environmental pollutants. The cytochrome P-450 enzymes and related microsomal enzymes not only metabolize foreign chemicals, but they also metabolize steroid hormones, sterols, fatty acids, prostaglandins and other lipid soluble normal body constituents. We have made great strides in understanding the biochemical properties, function, regulation and molecular biology of these enzymes (largely through the efforts of many of the investigators that we plan to have speak at this symposium). We are planning to bring together these scientists for discussions of their recent work and for a sharing of their efforts with others both by attendance at the meeting and through the publication that will follow the meeting. The result will be not only a sharing of ideas and education in the field of microsomes and the oxidation of foreign chemicals and normal body substrates, but the attendees should return to their laboratories, as they have after the six previous meetings, with new ideas and fresh enthusiasm to carry their work further.